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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/500,240	03/23/2005	Stefan Wildt	GFI/102	3290

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EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/500,240	WILDT ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 March 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) *1-60* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

This Application, filed March 23, 2005, is a 371 of PCT/US02/21510, filed December 24, 2002, and claims priority to U.S. Provisional Application 60/344,169, filed December 27, 2001.

Claims 1-60 are pending.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1-17, 46, drawn to a method for producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure, and to a human-like glycoprotein made by said method.

Group 2, claim(s) 1, 18, 19, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure, wherein the host cell is further deficient in expression of initiating alpha-1, 6 mannosyltransferase activity.

Group 3, claim(s) 1, 20, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure, wherein the host cell expresses GnTI UDP-GlcNAc transporter activities.

Group 4, claim(s) 1, 21, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure, wherein the host cell expresses a UDP- or GDP-specific diphosphatase activity.

Group 5, claim(s) 1, 22, 23, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure and further comprising a step of isolating the glycoprotein from the host and subjecting the isolated glycoprotein to at least one further glycosylation.

Group 6, claim(s) 1, 24-36, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure and further comprising a step of introducing into the host a nucleic acid molecule encoding one or more enzymes involved in the production of GlcNAcMan3GlcNAc2 or GlcNAc2Man3GlcNAc2.

Group 7, claim(s) 1, 37-40, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure and further comprising a step of introducing into a host a nucleic acid molecule encoding one or more enzymes for production of a GlcNAcMan4GlcNAc2 carbohydrate structure.

Group 8, claim(s) 1, 41-42, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure and further comprising a step of introducing into the host cell a nucleic acid molecule encoding one or more enzymes for production of a GlcNAc2Man3GlcNAc2 carbohydrate structure.

Group 9, claim(s) 1, 43, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure and further comprising a step of introducing into the host cell at least one nucleic acid molecule encoding at least one mammalian glycosylation enzyme.

Group 10, claim(s) 1, 44, drawn to a method of producing a human-like glycoprotein in a non-human eukaryotic host cell, comprising diminishing or depleting the activity of one or more enzymes in the host cell that transfers a sugar residue to the 1, 6 arm of a lipid-linked oligosaccharide structure and further comprising a step of transforming host cells with a DNA library.

Group 11, claim(s) 45, drawn to a host cell produced by the method of claim 1 or 44.

Group 12, claim(s) 47-49, drawn to a nucleic acid molecule comprising or consisting of at least 45 consecutive nucleotide residues of Fig. 6 (P. pastoris ALG3 gene).

Group 13, claim(s) 50, drawn to a P. pastoris cell in which the sequences of the P. pastoris ALG3 gene are mutated.

Group 14, claim(s) 51, drawn to a method to enhance the degree of glucosylation of lipid-linked oligosaccharides comprising the step of increasing alpha-1,3 glucosyltransferase activity in a host cell.

Group 15, claim(s) 52, drawn to a method to enhance the degree of glucosylation of lipid-linked oligosaccharides comprising decreasing the substrate specificity of oligosaccharyl transferase activity in a host cell.

Group 16, claim(s) 53, drawn to a method for producing in a non-mammalian host cell an immunoglobulin polypeptide.

Group 17, claim(s) 54, drawn to a non-mammalian host cell that produces an immunoglobulin having an N-glycan comprising a bisecting GlcNAc.

Group 18, claim(s) 55, drawn to an immunoglobulin having an N-glycan comprising a bisecting Glc-NAc.

Group 19, claim(s) 56, 58, drawn to a method for producing in a non-human host cell, a polypeptide having an N-glycan comprising a bisecting GlcNAc, the method comprising the step of expressing in the host cell a GnTIII activity and the polypeptide made by said method.

Group 20, claim(s) 57, drawn to a non-human host cell that produces a polypeptide having an N-glycan comprising a bisecting GlcNAc.

Group 21, claim(s) 59, drawn to a method for producing a human like-glycoprotein comprising the step of diminishing or depleting from the host cell an alg gene activity and introducing into the host cell at least on e glycosidase activity.

Group 22, claim(s) 60, drawn to a method for producing a human-like glycoprotein having an N-glycan comprising at least two GlcNacs attached to a trimannose core.

The inventions listed as Groups 1-22 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: unity of invention

between different catagories of inventions will only be found to exist if the specific combinations are present. These combinations include:

1) a product and special process of manufacture of said product,

2) a product and a process of use of said product,

3) a product, a special process of manufacture of said product, and a process of use of said product,

4) a process and an apparatus specially designed to carry out said process,

5) a product, a special process of manufacture of said product, and an apparatus specially designed to carry out said process.

The allowed combinations do not include multiple products, multiple methods of using said product, and methods of making multiple products as claimed in the instant application, see MPEP § 1850. In addition to this, Nakayama et al. 1992, The EMBO Journal, 11: 2511-2519 teach an OCH1 mutant in S. cerevisiae. The OCH1 mutant is an alpha-1,6 mannosyltranferase mutant (Nakayama et al., page 2516, 2nd col., 2nd parag.), which subsequently has the ability of making glycosylated proteins less like the yeast system and more like the mammalian system (see Cereghino and Cregg, 2000, FEMS Microbiology Reviews, 24: 45-66, see IDS; page 53, 2nd col. under "3.3 N-Linked Glycosylation").

Groups 1-22 are related to each other as each Group is either a method of making a mammalian protein with the appropriate sugar modifications found on mammalian protein, a cell used to make the protein, or the protein itself. However, the methods are distinct from each other as each requires different and distinct method

steps. The products are distinct from each other as each is structurally distinct from each other. A cell is structurally distinct from a protein and each of the cells claimed are distinct from each other as each is structurally and functionally distinct from each other.

The Application is further restricted as follows:

Should Group 1 be elected, methods comprising distinctly named enzymes, glycosidase or glycosyltransferase, in claim 6, are distinct inventions as each enzyme has distinct biological activity and one must be elected. The search and examination for a glycosidase and glycosyltransferase are burdensome because the searches are not coextensive.

Should Group 4 be elected, methods comprising distinctly named diphosphatases in claim 21 are distinct inventions and one must be elected. Each diphosphatase comprises a distinct structure and each has a distinct function. The search and examination for each diphosphatase are burdensome because the searches are not coextensive.

Should Group 6 be elected, methods comprising distinctly named sugars in claim 24 are distinct groups and one must be elected. Each sugar is distinct from the other because each has a distinct structure and different enzymes are required to make each. The search and examination for each sugar are burdensome because the searches are not coextensive.

In addition to electing a sugar for Group 6, methods comprising distinctly named enzymes used to make the elected sugar, listed in claims 25, 28, 30, are distinct inventions and one enzyme or a specific set of enzymes used to make the elected

sugar must be elected. The search and examination for each enzyme or set of enzymes used to make the sugar are burdensome because the searches are not coextensive.

Should Group 6 be elected, methods comprising the host cell expressing a diphosphatase, listed in claim 36, are distinct groups and one must be elected. Each diphosphatase is distinct because each has a specific biological activity. The search and examination for each diphosphatase is burdensome because the searches are not coextensive.

Should Group 7 be elected, methods comprising introducing a specific enzyme used in the production of GlcNAcMan4GlcNac2, as listed in claim 39, are distinct groups and one must be elected. Each enzyme comprises a distinct structure and each has a specific biological function. The search and examination for each enzyme is burdensome because the searches are not coextensive.

Should Group 7 be elected, methods further comprising introducing a nucleic acid encoding a mannosidase as listed in claim 40 are distinct groups and one must be elected. Each mannosidase comprises a distinct structure and each has a specific biological function. The search and examination for each enzyme is burdensome because the searches are not coextensive.

Should Group 9 be elected, methods further comprising introducing a nucleic acid molecules encoding a glycosylation enzyme listed in claim 43 are distinct groups and one must be elected. Each enzyme comprises a distinct structure and each has a

specific biological function. The search and examination for each enzyme is burdensome because the searches are not coextensive.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Group 1 is drawn to distinct N-glycans as listed in claim 5 and one must be elected. Each is distinct because each has a distinct biological activity. The search and examination for each are burdensome because the searches are not coextensive.

Group 1 is drawn to distinct glycosidases and glycotranferases in claim 7. One must be elected. Each is distinct because each has a distinct biological activity. The search and examination for each are burdensome because the searches are not coextensive.

Group 1 is drawn to distinctly named diminished or depleted enzymes in claims 8 and 9 and one must be elected. Each is distinct because each has a distinct biological activity. The search and examination for each are burdensome because the searches are not coextensive.

Group 1 is drawn to distinctly named sugar residues in claims 12-15 and one must be elected. Each sugar residue is distinct because each is structurally distinct from the other. The search and examination for each are burdensome because the searches are not coextensive.

Group 1 is drawn to distinctly named host cells in claim 17 and one must be elected. Each cell is distinct because each is structurally distinct from each other. The search and examination for each are burdensome because the searches are not coextensive.

Should Group 6 be elected and the enzyme, mannosidase of claim 25, be elected, Applicant is further required to elect an alpha-1,2-mannosidase derived from an organism. Each alpha-1,2-mannosidase is distinct as each has a distinct structure and distinct biological activity. The search and examination for each are burdensome because the searches are not coextensive.

Should Group 6 be elected and the enzyme glycosyltransferase of claim 28 be elected, Applicant is further required to elect a glycosyltransferase listed in claim 29. Each glycosyltransferase is distinct because each has a distinct biological activity. The search and examination for each glycosyltransferase is burdensome because the searches are not coextensive.

Should Group 6 be elected and fusion protein of claim 30 be elected, a fusion protein comprising a single targeting signal peptide as listed in claim 32 and a single catalytic domain, as listed in claim 33 is distinct and one signal peptide and one catalytic domain must be elected. Each fusion protein is distinct from each other because each comprises a signal peptide with a specific structure and function and a catalytic domain with a specific structure and function. The search and examination for each fusion protein combination is burdensome because the searches are not coextensive.

Should Group 7 be elected distinctly named mannosyltransferases as listed in claims 37 and 38 are distinct and one must be selected. Each mannosyltransferase is distinct because each comprises a distinct structure and each has a specific biological function. The search and examination for each mannosyltransferase is burdensome because the searches are not coextensive.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claim(s) are generic:

Claims 1-17, 46, of Group 1 are generic for N-glycans.

Claims 1-17, 46 of Group 1 are generic for glycosidases and glycotransferases.

Claims 1-17, 46 of Group 1 are generic for diminished or depleted enzymes.

Claims 1-14, 16, 17, 46 of Group 1 are generic for sugar residues.

Claims 1, 24-36 of Group 6 are generic for mannosidases.

Claims 1, 24-36 of Group 6 are generic for glycosyltransfereases.

Claims 1, 24-36 of Group 6 are generic for fusion proteins.

Claims 1, 37-40 of Group 7 are generic for mannosyltransferases.

The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the sugar groups and the proteins have been separated into species as each comprises distinct structures and each has different biological activity.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, Ph.D. can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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